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ADVANCEMENTS IN THE STUDY OF NON-CODING RNA'S ROLE IN MODULATING GLIOMA CHEMOTHERAPY RESISTANCE

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Abstract: Glioma represents the most frequently occurring malignant tumor of the human brain, constituting approximately 80% of all such cases. Its high malignancy, intense invasiveness, propensity for recurrence, and significant resistance to chemotherapy have significantly impacted the quality of life for patients affected by this disease. This article aims to provide a comprehensive overview of the research advancements made in understanding the mechanisms through which non-coding RNA regulates glioma's resistance to chemotherapy.
Keywords: Non-coding RNA; Glioma; Chemotherapy resistance

1 THE RESEARCH VALUE OF NON-CODING RNA

Among malignant central nervous system tumors, glioma is the most common type and one of the most malignant adult primary brain tumors with the worst prognosis. Treatment methods include surgery, radiotherapy and chemotherapy.. The growth location of glioma is very special, and its growth characteristics are mainly invasive. Current surgical treatment is difficult to remove completely, and it is easy to leave residual lesions, resulting in a high postoperative recurrence rate. Therefore, radiotherapy and chemotherapy have become important auxiliary treatments after surgery. However, during the treatment process, we often encounter another problem: resistance to chemotherapy drugs. Therefore, understanding the chemotherapy resistance process and its regulatory mechanisms from the molecular mechanism has become a research hotspot in the tumor community. With the application of shingled chips and new sequencing technologies, more than 90% of the proteins in the entire human genome sequence do not code but can be transcribed into RNA. These RNAs are non-coding RNAs [1]. It can regulate gene expression levels at multiple levels in the form of RNA. At the same time, the expression of non-coding RNA is different between normal tissues and tumor tissues, so it has become one of the targets of tumor gene therapy. This article collates recent research at home and abroad, and reviews the research value of non-coding RNA in glioma, the mechanism involved in chemotherapy resistance and the regulation of drug resistance, and the mechanism of chemotherapy resistance in glioma.

1.1 The Content of Non-Coding RNA is Higher than that of other Organs, which is Beneficial to Diagnosis and Prognosis Assessment

Compared with the content in other organs of the body, the expression content of non-coding RNA is higher in the central nervous system than in other peripheral organs. Because of this characteristic, glioma can be accompanied by differences in the expression of non-coding RNA during multiple development stages and multiple pathological changes. Li et al.[2] and Klein[3] mentioned that the expression content of Inc-RNA H19 is positively correlated with the grade of glioma. It is one of the key biological detection indicators for the progression of glioma, and it plays an important role in the progression of glioma. played a key role in its progress and invasion.

1.2 Non-Coding RNA is Involved in Multiple Biological Behaviors of Glioma Cells and is a Gene Target

The key to treatment lies in the cell proliferation, apoptosis and invasion of glioma cells. Non-coding RNA participates in the development of glioma through different transcriptional molecular mechanisms and signaling pathways. For example, CRNDE, another member of the non-coding RNA family, uses the mTOR signaling channel to play a regulatory role in glioma cell growth; in addition, Yin Shi et al.[4] also concluded through literature collection that ASLNC22381 and ASLNC20819 use IGF-1R to promote cell growth. Activation of proliferative signaling pathways.

1.3 Non-Coding RNA has Bidirectional Regulatory Function

The family of non-coding RNAs is very large, and each plays a different role. Some promote the occurrence and development of glioma, while others inhibit its proliferation and invasion. For example, Zhang et al. [5] found through experiments that in glioma patients, high expression of HOTAIR indicates a worse prognosis and survival rate; the expression levels of CRNDE in glioblastoma and astrocytoma are also higher than normal. Tissue is much higher. At the same time, this RNA also plays a role in promoting the proliferation and invasion of glioma.

2 MECHANISMS OF RESISTANCE TO CHEMOTHERAPY DRUGS IN GLIOMA

Currently, the chemotherapy drugs used for malignant glioma include cisplatin, temozolomide and nitrosourea drugs, as well as procarbazine, vinblastine and podophyllotoxin drugs, as well as molecular targeted drugs.

2.1 Cisplatin

Cisplatin is one of the most widely used chemotherapy drugs in clinical practice. It is often used in the chemotherapy treatment of solid tumors and is also used in the treatment of gliomas. However, cisplatin is prone to drug resistance during tumor treatment. Rabik et al. [6] The mechanism of drug resistance reaction discovered through clinical experiments is as follows: There is a drug transport system in cells, which can continuously transport drugs, so that the accumulated amount of cisplatin in the cells is continuously consumed; at the same time, tumor cells contain glutamine The expression of reducing substances such as thione can activate the drug detoxification system in the body. When the system is activated, the effective substances contained in the drug will be continuously removed; the repair of mismatches and cross-links occurs autonomously within the DNA. and other chain reactions, completely changing its mode of action and mechanism; apoptosis can also induce abnormalities in cell death pathways, etc.

2.2 Temozolomide

Temozolomide is a widely used chemotherapy drug in clinical practice. It is classified as a DNA alkylating agent. It can penetrate the blood-brain barrier and directly reach the tumor site. Its mechanism of action is to destroy DNA fragments in glioma cells and prevent them from carrying out DNA processing. Modification, causing tumor cells to undergo apoptosis or cause them to die. However, as the treatment process continues, patients will develop resistance to it, gradually reducing the sensitivity to the drug, making the treatment of the disease more difficult. Its drug resistance mechanism is related to the enhanced activity of methylguanine-DNA methyltransferase and nucleic acid mismatch repair protease; at the same time, its drug resistance mechanism is also a complex process involving multiple molecules.

2.3 Nitrosoureas

Nitrosourea drugs (Nus) are also one of the commonly used chemotherapy drugs for the treatment of glioma. They are alkylating agents. Its representative drugs are lomustine, carmustine, etc., which have the ability to penetrate the central nervous system. Highly lipid-soluble, it exerts anti-tumor effects mainly through alkylation damage to DNA. Jin Peng et al. [7] summarized the mechanisms of nitrosoureas chemotherapy resistance at home and abroad as follows: MGMT, BER, NER and MMR, which are involved in DNA damage repair in the human body and are involved in DNA damage repair, can also easily cause tumor chemotherapy resistance. Glutathione (GSH) and glutathione S-transferase (GST) present in the human body, in the process of protecting biological cells from damage by poisons (including cytotoxic drugs), also increase drug resistance during treatment.. But overall, Nus resistance is a very complex process.

3 CHEMOTHERAPY RESISTANCE MECHANISMS OF NON-CODING RNA

3.1 Regulatory Signaling Pathways and Tumor Chemotherapy Resistance

Non-coding RNA participates in important epigenetic processes such as genomic imprinting and chromatin remodeling, thereby changing the expression abundance of genes and affecting the expression of downstream drug resistance signaling pathways. At the same time, DNA epigenetic modifications also exist in non-coding RNA and mediate the regulation of other genes. Yang et al. [8] found through research that lncRNA AK126698 can promote the expression of NKD2 gene, and at the same time, NKD2 gene can inhibit Wnt/ The β-catenin signaling pathway allows non-small cell lung cancer cells to develop therapeutic resistance to cisplatin.

3.2 miRNA Interaction and Tumor Chemotherapy Resistance

For example, lncRNA ATB, a non-coding RNA, Shi et al.[9] found through research that it can become an endogenous competitive RNA (ceRNA) for miR-200c, and can promote the regulation of breast cancer cells by regulating related target genes. Lizumab forms a drug-resistant response and facilitates the invasion and migration of breast cancer cells in the body.

3.3 Regulating Drug Membrane Transport and Tumor Chemotherapy Resistance

Non-coding RNA can participate in regulating drug membrane transport by affecting the uptake and excretion of drugs, key metabolic enzymes and interfering with drug effects; research by Wang et al. [10] showed that knocking out lncR NAMRUL can promote doxorubicin and vincristine resistance. The drug increases the apoptosis of SGC7901/ADR and SGC7901/VCR in gastric cancer cell lines, allowing the drug to accumulate in cells. At the same time, it can also downregulate the expression of MRUL, thereby inhibiting the expression of ATP and subfamily B member 1 protein (ABCB1). Combined, it maintains the concentration balance of chemotherapy drugs in cells and dynamically regulates the sensitivity of tumor cells to chemotherapy drugs.

3.4 Apoptotic Proteins and Tumor Chemotherapy Resistance

During the course of chemotherapy, the adaptive changes of tumor cells, such as the transformation of epithelial cells into mesenchymal phenotype and the induction of CSC expansion, can cause chemotherapy resistance. In particular, EMT and CSC activation are closely related to drug resistance. Hang et al. [11] have shown that non-coding RNA has the potential to reverse EMT and regain the sensitivity of tumors to chemotherapy drugs. In addition, Wu et al. [12] found that since non-coding RNA does not undergo protein translation and mostly functions directly at the transcription level, it is also considered to have a more efficient "bridge regulatory effect".

4 CONCLUSION

The treatment of human brain glioma is one of the current treatment problems in the oncology community. How to find a drug with low resistance rate and good therapeutic effect is the direction that clinical oncologists have been working hard. With the deepening of clinical research and With the progress of non-coding RNA research, the mechanism of non-coding RNA in tumor drug resistance has gradually become clearer. However, currently, because the relationship between tumor chemotherapy resistance is complex and involves many pathways, it is difficult to discover its fundamental mechanism from the source. The mechanism of drug resistance and mechanism of action. The current mechanism of drug resistance of glioma chemotherapy is still debated by hundreds of schools of thought and is not very clear. At present, with the increasingly sophisticated research methods, the gradual discovery of non-coding RNA and its related regulatory signaling pathways will provide more effective methods for the treatment and diagnosis of glioma, and will also bring more hope to clinical patients. and the gospel.

COMPETING INTERESTS

The authors have no relevant financial or non-financial interests to disclose.

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